IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellants:	Jan E. Schnitzer and Philip Oh		
Application No.:	09/208,195	Group Art Unit:	1644
Filed:	December 9, 1998	Examiner:	P. Nolan
Confirmation No.:	7811		
For:	IMMUNOISOLATION OF CAVEOLAE		

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BRIEF ON APPEAL

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Sir:

This Brief on Appeal is submitted pursuant to the Notice of Appeal mailed on February 25, 2003, and received in the U.S. Patent and Trademark Office on March 3, 2003 in the above-referenced patent application. The fee for filing a brief in support of an appeal is enclosed. A Petition for Extension of Time and the appropriate fee are being filed concurrently.

This Brief is submitted in support of the appeal of the Examiner's final rejection of Claims 1-9, 11-17, 19-22, 24 and 25, as set forth in the Office Action made final, which was mailed from the Patent Office on November 25, 2002.

Each of the requirements set forth in 37 C.F.R. § 1.192(c) follow under the separate headings.

I. Real Party in Interest

The real parties in interest are the inventors Jan E. Schnitzer and Philip Oh. The rights, title and interest in the application were previously assigned to Beth Israel Deaconess Medical Center pursuant to an assignment by Jan E. Schnitzer and Philip Oh; however, Beth Israel Deaconess Medical Center subsequently released rights in the application back to the inventors.

II. Related Appeals and Interferences

Appellants and the undersigned Attorney are not aware of any related appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. Status of Claims

As filed, the instant application contained Claims 1 through 26. Claims 10, 18, 23 and 26 were canceled, and Claims 27-30 were added, in an amendment filed on October 3, 2000. Claims 27-30 were withdrawn from consideration by the Examiner in the Office Action dated January 2, 2001. Claims 1, 11, 19 and 24 were amended in an Amendment filed on June 4, 2001, in conjunction with a Request for Continued Examination (RCE).

In summary, Claims 1-9, 11-17, 19-22, 24, 25 and 27-30 are pending. Claims 1-9, 11-17, 19-22, 24, and 25 are the subject of this appeal.

IV. Status of Amendments

No Amendments after Final Rejection have been submitted. The pending claims are presented in the Appendix to this Brief.

V. Summary of Invention

Applicant's invention is drawn to methods of producing purified caveolae, the methods including an immunoisolation step of incubating a sample containing plasma membranes with an antibody that is specific for caveolin and which binds to oligomerized caveolin in its native state as an oligomeric structural cage surrounding intact caveolae. The methods are simple and efficient means of producing purified caveolae which closely resemble caveolae in their native

state (e.g., caveolae covered with the oligomeric structural cage of caveolin); the methods also minimize contamination and loss of molecules that dissociate from caveolae over time. Furthermore, the methods do not require perfusion of a tissue or coating of the plasma membranes with colloidal silica (described, for example, in US Patent 5,776,770), and thus allow a high level of flexibility of starting materials, as the methods can be used even for tissues or samples that cannot be perfused or coated with colloidal silica.

VI. Issues

Claims 1-9, 11-17, 19-22, 24 and 25 stand rejected under 35 U.S.C. 112, first paragraph. The following issue remains on appeal: whether the Examiner erred in stating that the claims were not enabled by the specification because the specification did not provide enablement for the use of an monoclonal antibody which binds oligomerized caveolin in its native state as an oligomeric structural cage surrounding intact caveolae, other than monoclonal antibody 2234.

VII. Grouping of Claims

The claims stand or fall together.

VIII. Argument

The methods of Appellants' invention utilize an immunoisolation step of incubating a sample with an antibody that is specific for caveolin and which binds to oligomerized caveolin in its native state as an oligomeric structural cage surrounding intact caveolae. Thus, Appellants' have described the essential characteristic of the antibody used in the isolation step. Methods for preparation of monoclonal and polyclonal antibodies are well-known to those of ordinary skill in the art; one of ordinary skill in the art would be able, using no more than routine experimentation, to generate antibodies that could have the characteristic of the antibody used in Appellants' invention. Furthermore, the Specification describes experiments by which the ability of an antibody to bind to caveolin in its native state as an oligomeric structural cage surrounding intact caveolae can be determined (see, e.g., p. 13, line 11 *et seq.*). Thus, one of ordinary skill in the art would be able to identify an antibody having the characteristic of the antibody used in the

invention, using routine experimentation comprising the methods described in the Specification to identify antibody having that feature. .

Appellants' disclosure describes the use of one antibody, CAV (also known as monoclonal antibody 2234), which is representative of a type of antibody with the specific characteristic set forth in the claims, namely, the ability to bind oligomerized caveolin in its native state as an oligomeric structural cage surrounding intact caveolae. The inability of other antibodies used in the experiments described in the disclosure, to bind to oligomerized caveolin in its native state as an oligomeric structural cage surrounding intact caveolae, does not indicate that undue experimentation would be necessary to identify other antibodies having the desired characteristics. Rather, it indicates only that those antibodies described in the experiments in the disclosure lack this particular characteristic and that a different antibody having this characteristic should be used in the methods of the invention.

In view of these considerations, one of ordinary skill in the art, given the state of the art regarding preparation of antibodies, having the description of the specific characteristic of the antibody (i.e., the ability to bind oligomerized caveolin in its native state as an oligomeric structural cage surrounding intact caveolae) set forth in the Specification, and also having possession of the methods of determining the binding characteristics of the antibody set forth in the Specification, would be able to identify other antibodies having the desired characteristics with no more than routine experimentation. Therefore, the claimed invention is enabled by the Specification.

CONCLUSION

In view of the discussion presented above, the claims as pending are fully enabled by the Specification. Therefore, it is respectfully requested that the rejection be reversed and that the claims be allowed.

Respectfully submitted,

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APPENDIX

What is claimed is:

1. (Amended) A method of producing purified caveolae, comprising the step of subjecting a sample of interest comprising plasma membranes to an immunoisolation method to separate caveolae from other materials in the sample of interest, wherein the immunoisolation method comprises incubating the sample of interest with a monoclonal antibody that is specific for caveolin and which binds to oligomerized caveolin in its native state as an oligomeric structural cage surrounding intact caveolae, and separating caveolae that are bound to the antibody from other materials in the sample of interest, thereby producing purified caveolae.

2. The method of Claim 1, wherein the sample of interest is selected from the group consisting of: cultured cells, cells isolated from a tissue, cell lysate, tissue, and microsomes derived from cells or from a tissue.

3. The method of Claim 1, wherein the sample of interest is a sample of plasma membranes.

4. The method of Claim 1, wherein the sample of interest is a disrupted plasma membrane sample.

5. The method of Claim 1, wherein the sample of interest is initial fractions of starting material that has been subjected to a separation method based on density.

6. The method of Claim 1, wherein the antibody that is specific for caveolin is attached to a solid phase.

7. The method of Claim 6, wherein the solid phase is magnetic beads.

8. The method of Claim 1, wherein the immunoisolation method comprises incubating the sample of interest with an antibody that is specific for caveolin for a time period that is less than approximately 2 hours,

9. The method of Claim 8, wherein the immunoisolation method comprises incubating the sample of interest with an antibody that is specific for caveolin for a time period that is equal to or less than approximately one hour.

11. (Amended) A method of producing purified caveolae, comprising the steps of:
providing a sample of interest comprising plasma membranes;

a) subjecting the sample of interest to a membrane disruption method, thereby producing a disrupted plasma membrane sample;

b) subjecting the disrupted plasma membrane sample to an immunoisolation method to separate caveolae from other materials in the disrupted plasma membrane sample, wherein the immunoisolation method comprises incubating the initial fractions with a monoclonal antibody that is specific for caveolin and which binds to oligomerized caveolin in its native state as an oligomeric structural cage surrounding intact caveolae, and separating caveolae that are bound to the antibody from other materials in the disrupted plasma membrane sample,

thereby producing purified caveolae.

12. The method of Claim 11, wherein the membrane disruption method of step (b) is shearing.

13. The method of Claim 11, wherein the membrane disruption method of step (b) is sonication.

14. The method of Claim 11, wherein the antibody that is specific for caveolin is attached to a solid phase.

15. The method of Claim 14, wherein the solid phase is magnetic beads.

16. The method of Claim 11, wherein the immunoisolation method comprises incubating the disrupted plasma membrane sample with an antibody that is specific for caveolin for a time period that is less than approximately 2 hours.

17. The method of Claim 16, wherein the immunoisolation method comprises incubating the disrupted plasma membrane sample with an antibody that is specific for caveolin for a time period that is equal to or less than approximately one hour.

19. (Amended) A method of producing purified caveolae, comprising the steps of:

a) providing a sample of interest comprising plasma membranes;

b) subjecting the sample of interest to a membrane disruption method, thereby producing a disrupted plasma membrane sample;

c) subjecting the disrupted plasma membrane sample to a separation method based on density, thereby producing fractions of the disrupted plasma membrane sample, and collecting initial fractions of the disrupted plasma membrane sample;

d) subjecting the initial fractions of the disrupted plasma membrane sample to an immunoisolation method to separate caveolae from the initial fractions, wherein the immunoisolation method comprises incubating the initial fractions with a monoclonal antibody that is specific for caveolin and which binds to oligomerized caveolin in its native state as an oligomeric structural cage surrounding intact caveolae, and separating caveolae that are bound to the antibody from other materials in the initial fractions,

thereby producing purified caveolae.

20. The method of Claim 19, wherein the separation method based on density of step (c) is sucrose density gradient centrifugation.

21. The method of Claim 19, wherein the immunoisolation method comprises incubating the initial fractions with an antibody that is specific for caveolin for a time period that is less than approximately 2 hours.

22. The method of Claim 21, wherein the immunoisolation method comprises incubating the initial fractions with an antibody that is specific for caveolin for a time period that is equal to or less than approximately one hour.

24. (Amended) A method of producing purified caveolae, comprising the steps of:

a) providing a sample of plasma membranes from cells of interest;

b) subjecting the sample of plasma membranes to a membrane disruption method, thereby producing a disrupted plasma membrane sample;

c) subjecting the disrupted plasma membrane sample to a separation method based on density, thereby producing fractions of the disrupted plasma membrane sample, and collecting initial fractions of the disrupted plasma membrane sample;

d) subjecting the initial fractions of the disrupted plasma membrane sample to an immunoisolation method to separate caveolae from the initial fractions, wherein the immunoisolation method comprises incubating the initial fractions with a monoclonal antibody that is specific for caveolin and which binds to oligomerized caveolin in its native state as an oligomeric structural cage surrounding intact caveolae, for a time period that is less than approximately 2 hours, and separating caveolae that are bound to the antibody from other materials in the initial fractions,

thereby producing purified caveolae.

25. The method of Claim 24, wherein the immunoisolation method comprises incubating the initial fractions with an antibody that is specific for caveolin for a time period that is equal to or less than approximately one hour.

27. Purified caveolae prepared by a method comprising the step of subjecting a sample of interest comprising plasma membranes to an immunoisolation method to separate

caveolae from other materials in the sample of interest, wherein the immunoisolation method comprises incubating the sample of interest with an antibody that is specific for caveolin and which binds to oligomerized caveolin, and separating caveolae that are bound to the antibody from other materials in the sample of interest.

28. Purified caveolae prepared by a method comprising:

a) providing a sample of interest comprising plasma membranes;

b) subjecting the sample of interest to a membrane disruption method, thereby producing a disrupted plasma membrane sample;

c) subjecting the disrupted plasma membrane sample to an immunoisolation method to separate caveolae from other materials in the disrupted plasma membrane sample, wherein the immunoisolation method comprises incubating the initial fractions with an antibody that is specific for caveolin and which binds to oligomerized caveolin, and separating caveolae that are bound to the antibody from other materials in the disrupted plasma membrane sample.

29. Purified caveolae prepared by a method comprising:

a) providing a sample of interest comprising plasma membranes;

b) subjecting the sample of interest to a membrane disruption method, thereby producing a disrupted plasma membrane sample;

c) subjecting the disrupted plasma membrane sample to a separation method based on density, thereby producing fractions of the disrupted plasma membrane sample, and collecting initial fractions of the disrupted plasma membrane sample;

d) subjecting the initial fractions of the disrupted plasma membrane sample to an immunoisolation method to separate caveolae from the initial fractions, wherein the immunoisolation method comprises incubating the initial fractions with an antibody that is specific for caveolin and which binds to oligomerized caveolin, and separating caveolae that are bound to the antibody from other materials in the initial fractions.

30. Purified caveolae prepared by a method comprising:

a) providing a sample of plasma membranes from cells of interest;

b) subjecting the sample of plasma membranes to a membrane disruption method, thereby producing a disrupted plasma membrane sample;

c) subjecting the disrupted plasma membrane sample to a separation method based on density, thereby producing fractions of the disrupted plasma membrane sample, and collecting initial fractions of the disrupted plasma membrane sample;

d) subjecting the initial fractions of the disrupted plasma membrane sample to an immunoisolation method to separate caveolae from the initial fractions, wherein the immunoisolation method comprises incubating the initial fractions with an antibody that is specific for caveolin and which binds to oligomerized caveolin, for a time period that is less than approximately 2 hours, and separating caveolae that are bound to the antibody from other materials in the initial fractions.